REMARKS

This is in response to the Final Office Action dated December 31, 2002 (Paper No. 11) and the Advisory Action dated June 16, 2003 (Paper No. 14) which issued in the parent application (U.S.S.N. 09/658,734).

Claims 13, 14, and 23-32 were pending in the present application. Claims 14 and 23 have been canceled, without prejudice, claims 13, 24, 29, and 30-32 have been amended, and new claims 33-71 have been added. Accordingly, after the amendments presented herein have been entered, claims 13 and 24-71 will remain pending.

Support for the new claims and the claim amendments presented herein can be found throughout the specification, including the originally filed claims. Support for new claims 68-71 may be found in the specification at least, for example, page 20, line 28 and at page 14, line 30 through page 15, line 13.

No new matter has been added. Any amendments to and/or cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Rejection of Claims 13-14 and 23-32 Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 13-14 and 23-32 under 35 U.S.C. §112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." In particular, the Examiner is of the opinion that

> [c]laims 13, 30, 31, 32 and their dependents are drawn to a method for identifying a contraceptive or compound which modulates meiosis, however are rendered vague and indefinite for reciting "said compound" in step d because it is unclear id "said compound" is referring to the test compound of steps a and b, or the selected compound of step c. Applicant may prefer to insert the word "selected" between "said" and "compound" or step d, to more clearly identify which compound is identified as the compounds useful as a contraceptive or modulator of meiosis.

Applicants' gratefully acknowledge the Examiner's indication in the Advisory Action dated June 16, 2003 that the instant rejection has been overcome by the Applicants' Amendment and Response filed on June 2, 2003 (Paper No. 12). However, in an effort to provide a complete response to the Final Office Action (Paper No. 11) issued in the parent application, Applicants reiterate the comments set forth in the prior filed Amendment and Response (Paper No. 12) regarding the instant rejection as follows:

Applicants respectfully traverse the foregoing rejection. However, in an effort to expedite prosecution and in no way acquiescing to the Examiner's rejection, Applicants have amended claims 13 and 30 as suggested by the Examiner. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

With respect to claim 30 and the Examiner's is statement that this claim "is rendered vague and indefinite for reciting 'modulates' in step c, because it is unclear what activity must occur for the compound to qualify as a contraceptive. For example, does the compound inhibit, stimulate, destroy, or deactivate MSH5."

Applicants respectfully traverse the foregoing rejection. Applicants respectfully submit that the claim language is clear and definite and would be understood by one of skill in the art when read in combination with the teachings of the specification. The meaning of the term "modulates" would have been readily apparent to one of ordinary skill in the art at the time the instant application was filed in view of the teachings of Applicants' specification and the well-established meaning of the term. Modulation, *e.g.*, of MSH5 expression or activity, would have been readily understood by one of ordinary skill in the art to mean either the inhibition of expression or activity or the stimulation of expression or activity. Applicants' specification, at page 14, lines 30-35 identifies "modulators" as compounds which "have a stimulatory or inhibitory effect on, for example, MSH5 expression or MSH5 activity." Accordingly, the meaning of the term "modulation" was well-established in the art at the time of filing of the

instant application and its' meaning would have been readily apparent to one of skill in the art in view of Applicants' specification.

However, in the interest of expediting prosecution, and in no way acquiescing to the Examiner's rejection, claim 30 has been amended such that it contains the term "inhibition" rather than the term "modulation." Accordingly, the pending claims comply with 35 U.S.C. §112, second paragraph. Based on the foregoing, Applicants' respectfully request reconsideration and withdrawal of the foregoing rejection.

Rejection of Claims 31 and 32 Under 35 U.S.C. §103(a)

The Examiner has rejected claims 31 and 32 under 35 U.S.C. §103(a) as being unpatentable over Fishel *et al.* (U.S. Patent No. 6,333,153) in view of Winand *et al.* In particular, the Examiner is of the opinion that

> Fishel teaches a method for determining if a composition (test compound) affects (or modulates) expression of a gene encoding a MutS homolog (MSH) (col. 9 line 10-15) wherein the MutS homolog may be MSH5 (col. 4 line 35-40). The method comprises administering the test composition (or compound) to a cell containing the MutS homolog (or MSH5) and a cell which does not contain the MutS homolog followed by observing phenotypic effects on the cells to determine if the compound effects (or modulates) MutS homolog activity (col. 9 line 29-45). Fishel does not teach the method wherein the test compound that modulates MSH5 is useful for modulating meiosis. However, Winand teaches that MSH5 is required in normal meiotic crossing over (abstract, p. 69 right column) and encodes proteins which function in meiotic cells (p. 69, right column). Moreover, at the time of the claimed invention, it was known in the art that MSH5 plays a modulating role in meiosis. Therefore, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to identify meiosis-modulating-compounds by identifying compounds which modulate MSH5. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by Winand to use the methods of Fishel for identifying compounds which modulate MSH5, with a reasonable expectation for successfully identifying compounds which modulate meiosis. Applicant argues that the references do not teach a relationship between MSH5 and meiosis modulation. However, this argument fails to persuade because as disclosed by Winand, it was known in the art that MSH5 plays a crucial role in meiosis, as stated above.

Applicants respectfully traverse the foregoing rejection. Specifically, Fishel *et al.* fail to teach or suggest ***any*** association between MutS homologs, such as MSH5, and contraception or meiosis. Nor do Fishel *et al.* teach or suggest methods for identifying candidate compounds useful for modulating, *e.g.*, inhibiting meiosis. Thus, the primary reference of Fishel *et al.* relied upon by the Examiner fails to teach or suggest the claimed invention.

Furthermore, Applicants respectfully submit that the secondary reference of Winand *et al.* relied on by the Examiner fails to make up for the above stated deficiencies in the primary reference of Fishel *et al.* Specifically, Winand *et al.* disclose identification of the nucleotide and amino acid sequences of *C. elegans* and human MSH5.

Winand *et al.* state that ***S. cerevisiae*** MSH5 is required for "normal levels of meiotic crossing over" (page 69, right column). As is known in the art, homology between yeast and human proteins alone is insufficient to determine the function of a molecule. Winand *et al.* does not conclusively set forth any function of the human MSH5 molecule. As set forth in Winand *et al.* "much of the anaylsis of higher eukaryotic MSH genes has been focused on the MSH2, MSH3, and MSH6 genes," which are involved in mismatch repair, and not on MSH5. With respect to human MSH5, while Winand *et al.* make the ***general*** statement that, ***based on only expression data***, human MSH5 ***may*** be important for a meiosis-specific process like recombination (see page 77, right column), Winand *et al.* do not conclusively show involvement of MSH5 in meiosis, in contrast to the teachings of Applicants' specification (see, for example, Example 1 of Applicants' specification). ***Furthermore, nowhere do Winand et al. teach or suggest methods for identifying candidate compounds useful for modulating meiosis in a cell.*** Thus, Winand *et al.*, in combination with Fishel *et al.* fail to teach or suggest Applicants' invention.

However, in traversal of the instant rejection, Applicants hereby submit unexecuted declarations under 37 C.F.R. §1.131 (referred to here in as "the declarations"). Applicants' respectfully submit that we are in the process of obtaining executed declarations under 37 C.F.R. §1.131, which will be submitted as soon as possible.

It is Applicants' position that the declarations submitted herewith obviate the Examiner's rejection of claims 31 and 32 based on Fishel and Winand *et al.* As described in the declarations, conception of Applicants' invention as set forth in claims 31 and 32 was completed in this country prior to October 1, 1998, which is the publication date of the Winand *et al.* reference. The publication date of the Winand *et al.* reference is evidenced by the attached printout from the Science Direct website which indicates a date of October 1, 1998 for the volume 53, Issue 1 of Genomics in which the Winand *et al.* reference appeared. The Examiner is relying on Winand, *et al.* as teaching that "MSH5 is required in normal meiotic crossing over. . . and encodes proteins which function in meiotic cells." However, as set forth in the declarations, the manuscript attached as Appendix A, which was authored by the inventors of the instant application, describes experiments which are the basis of the instant application, including the generation of mice carrying a null mutation in the MHS5 gene, and the finding that mice homozygous for this mutation are viable but are sterile. The manuscript specifically discloses that MSH5 is essential for normal meiosis. Furthermore, as stated in the declarations, based on the observation that mice carrying a null mutation in the MHS5 gene and the identification of the role of MSH5 in meiosis, the inventors conceived of the usefulness of MSH5 in screening assays for identifying inhibitors of meiosis, as is presently claimed, prior to October 1, 1998. Thus, conception of the invention described and claimed in rejected claims 31 and 32 was completed in this country prior to October 1, 1998.

Accordingly, based on the foregoing, Winand *et al.* is not available for use by the Examiner as a reference, either basic or auxiliary, in the rejection of the claims of the instant application. As set forth above, Fishel *et al.* alone fail to teach or suggest any association between MutS homologs, such as MSH5, and meiosis or contraception. Fishel *et al.* also fail to teach or suggest methods for identifying candidate compounds useful as contraceptives or useful for modulating meiosis. Thus, Fishel *et al.* alone fails to teach or suggest the claimed invention.

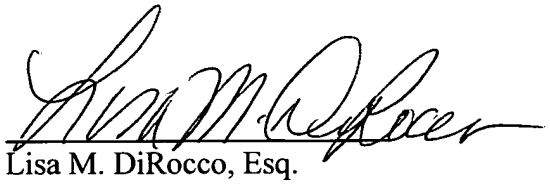
Accordingly, Applicant respectfully request reconsideration and withdrawal of the rejection of claims 31 and 32 under 35 U.S.C. §102(a) and/or 35 U.S.C. §103(a).

CONCLUSION

In view of the amendments set forth above, it is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

Respectfully submitted,

LAHIVE & COCKFIELD, LLP



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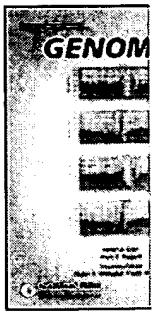

Gérard Goubin, John Fawcett, Scott Cram, Bernard Dutrillaux, Sam Hanash and Martine Muleris
Abstract | Abstract + References | PDF (2797 K)

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6. ☐ **Organization and Evolution of Olfact ry Receptor Genes on Human Chromosome 11[*1]**, *Pages 56-68*
Jill A. Buettner, Gustavo Glusman, Nissim Ben-Arie, Purita Ramos, Doron Lancet and Glen A. Evans
Abstract | Abstract + References | PDF (904 K)

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7. ☐ **Cloning and Characterization of the Human and*Caenorhabditis elegans*Homologs of the*Saccharomyces cerevisiae MSH5*Gene[*1]**, *Pages 69-80*
Nena J. Winand, Jessica A. Panzer and Richard D. Kolodner
Abstract | Abstract + References | PDF (443 K)

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8. ☐ **Characterization of Two Novel Protocadherins (*PCDH8*and*PCDH9*) Localized on Human Chromosome 13 and Mouse Chromosome 14[*1]**, *Pages 81-89*
Sabine Strehl, Karen Glatt, Qiu Mei Liu, Heather Glatt and Marc Lalande
Abstract | Abstract + References | PDF (2474 K)

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9. ☐ **Characterization of a Human Homologue of the*Saccharomyces cerevisiae*Transcription Factor Spt3 (SUPT3H)[*1]**, *Pages 90-96*
Jianming Yu, Jon M. Madison, Stephan Mundlos, Fred Winston and Bjorn R. Olsen
Abstract | Abstract + References | PDF (437 K)

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10. ☐ **Identification of Two*Krüppel*-Related Zinc Finger Genes (*ZNF200*and*ZNF210*) from Human Chromosome 16p13.3[*1, *2]**, *Pages 97-103*
Zuoming Deng, Michael Centola, Xiaoguang Chen, Raman Sood, Anil Vedula, Nathan Fischel-Ghodsian and Daniel L. Kastner
Abstract | Abstract + References | PDF (1458 K)

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11. ☐ **Human ARHGDIG, a GDP-Dissociation Inhibitor for Rho Proteins: Genomic Structure, Sequence, Expression Analysis, and Mapping to Chromosome 16p13.3[*1]**, *Pages 104-109*
Chaker N. Adra, Anand R. Iyengar, Farzand A. Syed, Imaduddin N. Kanaan, Koji Abe, Horacio L. R. Rilo, Weijiang Yu, Reshma Kheraj, Shin R. Lin, Tadashi Horiuchi *et al.*
Abstract | Abstract + References | PDF (1502 K)

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12. ☐ **Genomic Structure and Physical Mapping of*C17orf1:*A Gene Associated with the Proximal Element of the CMT1A-REP Binary Repeat[*1]**, *Pages 110-112*
Marina L. Kennerson, Najah T. Nassif and Garth A. Nicholson

Abstract | Abstract + References | PDF (64 K)

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13. ☐ **Isolation of a Microsatellite That Reveals Paralogy between the Subtelomeric Regions of Mouse Chromosomes 17 and 19: Further Evidence for Telomere–Telomere Exchange in the Mouse,** *Pages 113-114*
D. M. Chambers, D. Kipling and C. M. Abbott
Abstract | Abstract + References | PDF (44 K)

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14. ☐ **Isolation of the Human Beaded-Filament Structural Protein 1 Gene (*BFSP1*) and Assignment to Chromosome 20p11.23–p12.1[*1],** *Pages 114-116*
Nanna D. Rendtorff, Claus Hansen, Asli Silahtaroglu, Karen F. Henriksen and Niels Tommerup
Abstract | Abstract + References | PDF (153 K)

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15. ☐ **Testis β-1,4-Galactosyltransferase Gene Maps to Mouse Chromosome 5[*1],** *Pages 117-118*
Tadashi Kaname, Kazuyoshi Uehara, Kuniya Abe, Takashi Muramatsu and Ken-ichi Yamamura
Abstract | Abstract + References | PDF (58 K)

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16. ☐ **Radiation Hybrid Mapping of the Human MN/CA9 Locus to Chromosome Band 9p12–p13,** *Pages 118-119*
Yoshinori Nakagawa, Hirotsugu Uemura, Yoshihiko Hirao, Katsunori Yoshida, Shinsuke Saga and Kazuhiro Yoshikawa
Abstract | Abstract + References | PDF (52 K)

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17. ☐ **Localization of the Type 3 Iodothyronine Deiodinase (*DIO3*) Gene to Human Chromosome 14q32 and Mouse Chromosome 12F1[*1],** *Pages 119-121*
Arturo Hernandez, Jonathan P. Park, Gholson J. Lyon, Thuluvancheri K. Mohandas and Donald L. St. Germain
Abstract | Abstract + References | PDF (123 K)

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